

THE CARBOHYDRATES

Chemistry and Biochemistry

SECOND EDITION

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We dedicate this work to the persons most responsible for our professional development

HORACE S. ISBELL AND THE LATE MELVILLE L. WOLFROM

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9. GLYCOSIDES

W. G. OVEREND

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I. INTRODUCTION

The designation *glycoside* is used for the acetal derivatives of the cyclic forms of sugars in which the hydrogen atom of the hemiacetal hydroxyl group has been replaced by an alkyl, aralkyl, or aryl group. In this restricted sense, glycosides are mixed, monocyclic acetals. On complete hydrolysis they afford a mono- or polyhydric alcohol or phenol, and one or more monosaccharides. Glycosides derived from aldoses are referred to as aldoses, and those from ketoses are ketosides. In aldoses and ketosides the ring-oxygen atom is connected to C-1 and C-2, respectively, of the sugar.

Thioglycosides may be regarded as derivatives of 1-thio sugars, but frequently they are defined as 1-thioglycosides to differentiate them from glyco-

sides of a thio sugar in which the thiol group is located in the parent sugar at a site other than C-1.

For convenience, the alkyl, aralkyl, or aryl group is referred to as the "aglycon group," and the corresponding alcohol (or thiol) or phenol (or thiophenol) is called the "aglycone." The sugar residue is the "glycosyl" group ("glycofuranosyl" or "glycopyranosyl" for five- and six-membered rings, respectively).

The term glycoside is used in the generic sense, and specific glycosides are named by replacing the ending "ose" of the parent sugar by "oside," and by adding the name of the alkyl or other radical and the symbol α or β to designate the configuration of the glycosidic (anomeric) carbon—for example, methyl α -D-xylofuranoside or phenyl β -D-glucopyranoside.

For complex groups, it is sometimes more convenient to use the name of the alcohol or phenol rather than the radical, as in hydroquinone α -D-galactopyranoside. *p*-Hydroxyphenyl β -D-glucopyranoside may also be named catechol β -D-glucopyranoside. When several hydroxyl groups in polyhydric alcohols or phenols are linked glycosidically, the nomenclature is not uniform. For natural glycosides phytochemical names are used frequently, although chemical names are preferable because they indicate structure and facilitate classification. The trivial names have the advantage of brevity and indicate the source of the glycoside, as, for example, salicin (*o*-hydroxymethylphenyl β -D-glucopyranoside) from the bark of willow (*Salix helix*).

Di-, oligo-, and polysaccharides have glycosidic linkages, the aglycon group being a sugar residue. Many of these higher saccharides have trivial names.

The nomenclature of 1-thioglycosides is analogous to that given for glycosides in general.

This Chapter is limited to an account of aspects of the chemistry of simple glycosides of the type described, and, although such simple glycosides undergo numerous reactions at sites in the molecule other than the anomeric center, only reactions involving the glycosidic linkage will be described.

Mention should be made of usage of the term "glycoside" in a wider context nowadays than is covered by the subject matter of this Chapter. Glycosan, in which acetalation has taken place within an aldose molecule to produce an internal bicyclic acetal, are regarded as inner glycosides. Ketohexoses form bimolecular dianhydrides containing a central *p*-dioxane ring, in which the glycosidic center of each sugar residue is linked to an oxygen atom of the central ring.

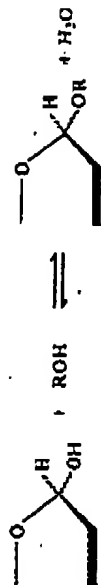
Glycosides are widely distributed in Nature, particularly in plants. Because the chemistry of the natural glycosides resides to a considerable degree in the aglycon residue, and in biochemical relationships, they are described separately in Vol. IIA, Chapters 32 and 33.

II. METHODS FOR SYNTHESIS

Although many methods for the synthesis of glycosides have been studied, relatively few have found wide or general application. Most of the individual procedures are restricted to a certain aglycon type and often depend also on the nature of the glycone undergoing glycosidation. General preparative methods for methyl and phenyl glycosides have been reviewed.¹

A. FISCHER METHOD

Aldehydes or ketones react in anhydrous alcoholic solutions of hydrogen chloride to form acetals. The simplest members of the sugar series, glyceraldehyde and glycenedehyde, react similarly. In attempting to synthesize acetals of higher sugars by treating them with methanol and hydrogen chloride, Fischer² found that only one methyl group was introduced per mole of sugar and that a methyl glycoside was formed. The sugars in their cyclic forms (hemiacetals) establish an equilibrium in the reaction medium, in which



anomeric glycopyranosides and glycofuranosides preponderate. The formation and hydrolysis of glycosides is a reversible reaction, but, as carried out in practice, the reaction is forced in one direction as far as possible, by use of a large excess of alcohol or of water.

The Fischer synthesis, which is applicable with alcohols but not with phenols, is particularly suited to the preparation of glycosides with lower aliphatic alcohols. Disaccharides frequently undergo alcoholysis of the linkage between the constituent residues, and *O*-acetyl groups of acetylated sugars are hydrolyzed. The customary procedure is to heat a solution or suspension of the monosaccharide in the alcohol in the presence of a few percent of hydrogen chloride as catalyst. The furanoid forms of the sugars react most readily, but pyranosides are generally the principal constituents under equilibrium conditions, and so by appropriate selection of reaction conditions preponderant formation of either pyranosides or furanosides can be achieved (see p. 282).

¹ References start on p. 346.